SERIOUS ADVERSE EVENTS REPORTING

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Overview

- **Important definitions**
- **Review key features of the NMCP Serious Adverse Events (SAE) Reporting Policy**
- **Questions and discussion**

What is an Adverse Event (AE)?

- Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign, symptom, or disease, temporally associated with the subject's participation in the research, whether or not considered related to the subject's participation in the research.
- An AE may be expected or unexpected, related or unrelated to the subject's participation in the research, local or non-local, and serious or not serious.
- The study investigator is responsible for determining the status of an event.

AE Definitions cont.

An *Unexpected* event is one in which the nature, severity, or frequency of the event is *not* consistent with any of the following:

(a) Investigator's Brochure,
(b) Investigation plan or application,
(c) IRB approved research protocol,
(d) IRB approved informed consent document,
(e) Product labeling and package inserts,
(f) HIPAA Authorization document, or
(g) the reasonably expected natural history and progression of the underlying disease or condition

AE Definitions cont.

The relatedness of an event falls into one of three categories:

- A ***Related*** event is one for which there is reasonable information (e.g., strong temporal relationship, clinical indication) that the event may have been at least partially caused by the procedures involved in the research.

- A ***Possibly Related*** event means there is a reasonable possibility that the event, incident, experience, or outcome may have been caused by the procedures involved in the research; however, there is insufficient information to determine the likelihood of this possibility.

- An ***Unrelated*** event is one where there is no information or reason to attribute the event or problem to procedures involved in the research.

AE Definitions cont.

Events are also identified by location:

- A ***Local*** event occurs when the adverse event or incident is experienced by a subject participating in a study here at NMCP.

- A ***Non-local*** event occurs when the adverse event or incident is experienced by a subject participating in a study being conducted at an institution outside of NMCP (as is the case in a multi-center trial).

What is a Serious Adverse Event (SAE)?

An *SAE* is an event that results in any of the following outcomes:

(1) fatal (death);

(2) life-threatening;

(3) inpatient hospitalization or prolongation of existing hospitalization;

(4) persistent or significant disability/incapacity;

(5) congenital anomalies or birth defect; or

(6) any other adverse event that, based upon appropriate medical judgment, may jeopardize the subject's health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition

Unanticipated Problems (UP) Involving Risks to Subjects or Others

An UP is defined as any incident, experience, or outcome that meets all of the following criteria:

(1) *Unexpected* (in terms of nature, severity, or frequency) given

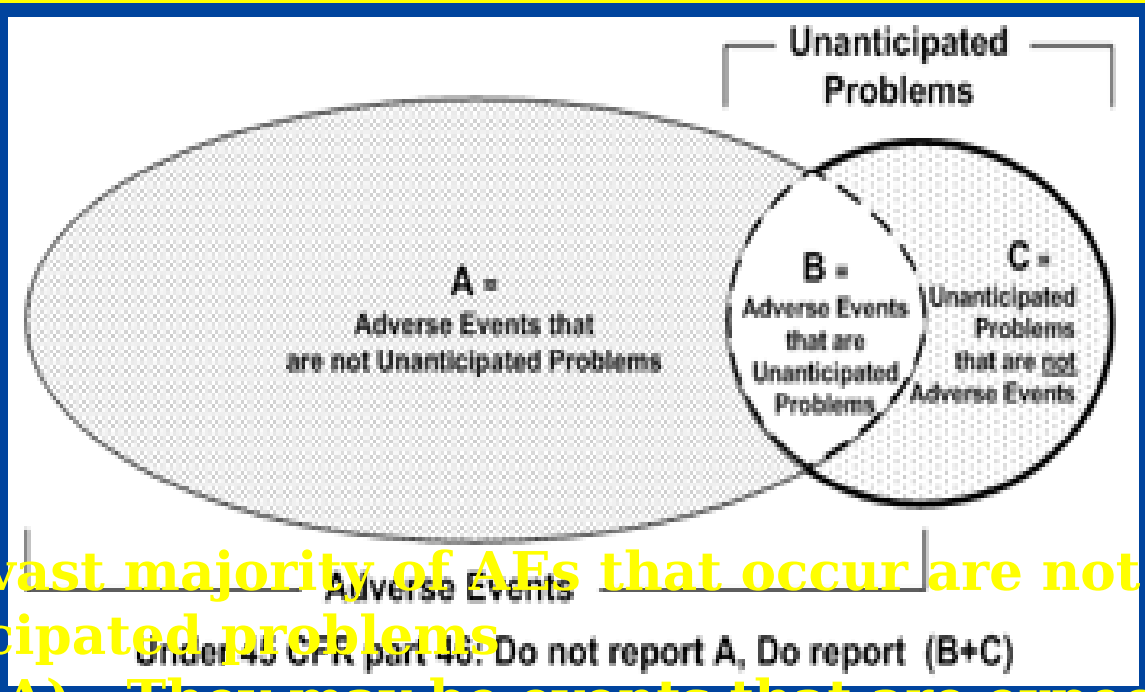
(a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and

(b) the characteristics of the subject population being studied;

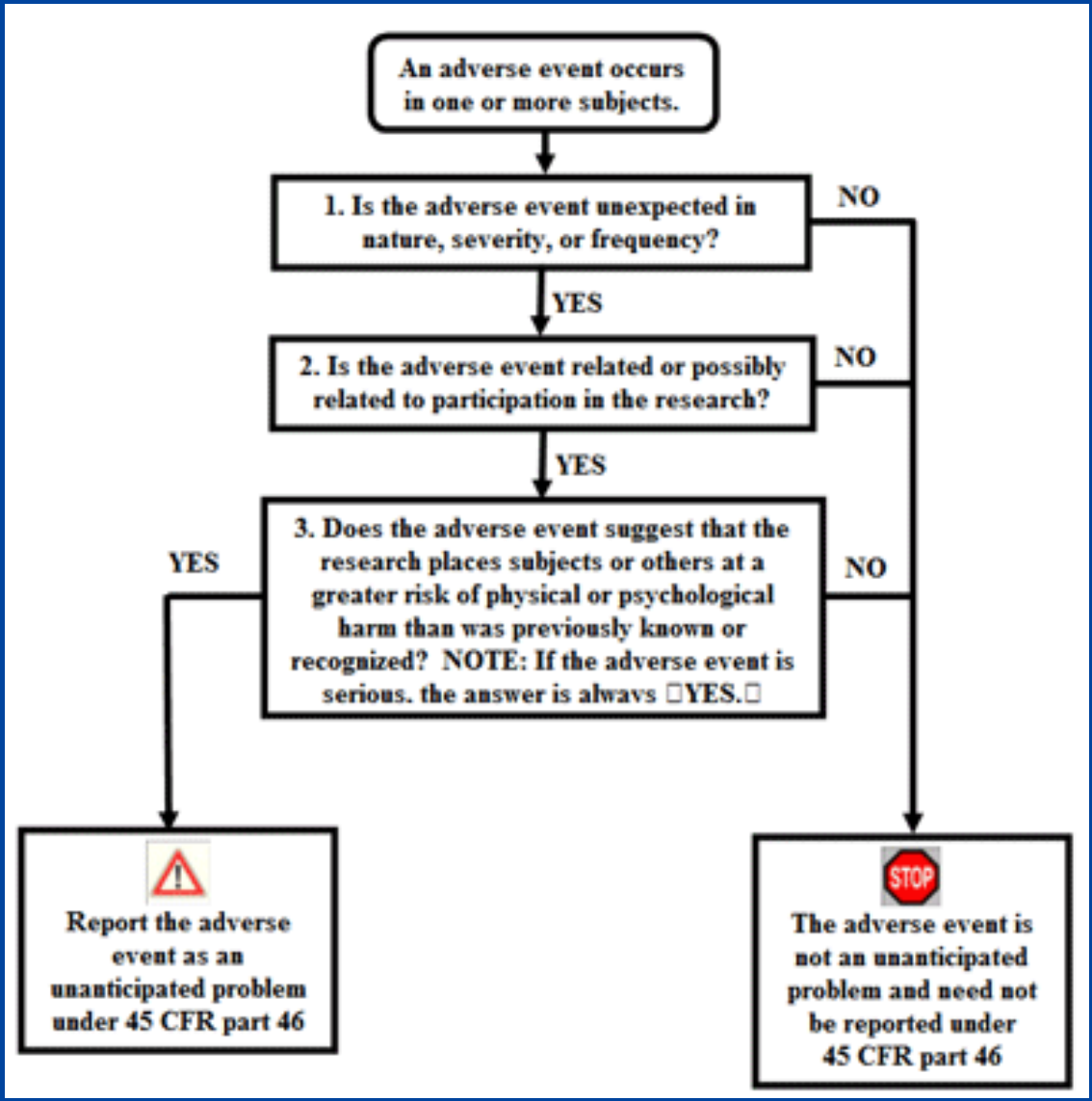
(2) *Related or Possibly Related* to participation in the research (possibly related means there is a reasonable possibility that the incident, experience or outcome may have been caused by the procedures involves in the research); and

(3) Suggests that the research places subjects or others at *a greater risk of harm* (including physical, psychological, economic, or social harms) related to the research than was previously known or recognized.

Relationship between Adverse Events and Unanticipated Problems:


Unanticipated Problems
A =
Adverse Events that are not Unanticipated Problems
B =
Adverse Events that are Unanticipated Problems
C =
Unanticipated Problems that are not Adverse Events
Adverse Events
Under 45 CFR part 46: Do not report A, Do report (B+C)

- The vast majority of AEs that occur are not unanticipated problems (Area A). They may be events that are expected, for example.
- A smaller proportion of AEs are unanticipated problems (Area B). These events are unexpected, serious, related to the research, and suggest additional risk to subjects or others.
- Unanticipated problems include other incidents, experiences, and outcomes that are not AEs (Area C). UPs that are not


An adverse event occurs in one or more subjects.
1. Is the adverse event unexpected in nature, severity, or frequency?
NO
YES
2. Is the adverse event related or possibly related to participation in the research?
NO
YES
3. Does the adverse event suggest that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized? NOTE: If the adverse event is serious. the answer is alwavs □YES.□
YES
NO
Report the adverse event as an unanticipated problem under 45 CFR part 46
STOP
The adverse event is not an unanticipated problem and need not be reported under 45 CFR part 46

Algorithm for determining whether an AE represents an UP that needs to be reported

NMCP Reporting Policy

The NMCP IRB Standard Operating Procedures (SOPs) define the reporting policy for adverse events/unanticipated problems.

- **If a local event is identified as an SAE (unexpected, serious, and related) it must be reported to the IRB within 5 days of discovery.**
- **If the SAE involves a local death, it must be reported to the IRB within 1 day of discovery.**
- **Reporting may be accomplished by telephone, fax, or email.**
- **The appropriate forms, reports, and documents must be submitted to the IRB within 5 days of reporting.**

NMCP Reporting Policy cont.

Materials for IRB review of a local SAE include:

- ***SAE/Unanticipated Problem Form*** **(found on the CID webpage)**
- **Report by the Medical Monitor**
- **Supplemental documents as appropriate, such as:**
  - **Data Safety Monitoring Board (DSMB) report;**
  - **Follow-up report on the subject's condition;**
  - **Proposed changes to the study protocol or consent form resulting from the event; or**
  - **A corrective action plan to prevent future occurrences.**

NMCP Reporting Policy cont.

Materials for review of a non-local SAE include:

- ***Report Non-Local Serious Adverse Event or Safety Report*** **form (found on the CID webpage)**
- **Copy of the Safety Report received from the multi-center sponsor (pharmaceutical company, etc.) or the multi-center cooperative (COG, RTOG, GOG, etc.)**
- **Supplemental documents as appropriate, such as**
  - **DSMB report;**
  - **Statement from the investigator about local**

NMCP Reporting Policy cont.

The IRB requires submission of *serious adverse events* <u>only</u>.

Please contact CID for guidance if the investigator of a local study or the sponsor of a multi-center trial requires IRB acknowledgement of *adverse events*.

Questions?

For more information about adverse events or reporting requirements, please refer to the NMCP IRB SOPs or contact CID at (757) 953-5939.